Advance journal of pharmaceutical research & review
Volume 1, Issue I, May 2024, PP.16-21
www.ajprr.com e -ISSN: 3048-491X

Formulation and Evaluation of Sustained Release Matrix Tablets of Glipizide

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ABSTRACT

I. Background: Glipizide, sold under the brand name Glucotrol among others, is an anti-diabetic medication of the sulfonylurea class used to treat type 2 diabetes.It is used together with a diabetic diet and exercise.It is not indicated for use by itself in type 1 diabetes. It is taken by mouth. Effects generally begin within half an hour and can last for up to a day.

Common side effects include nausea, diarrhea, low blood sugar, and headache. Other side effects include sleepiness, skin rash, and shakiness. The dose may need to be adjusted in those with liver or kidney disease. Use during pregnancy or breastfeeding is not recommended. It works by stimulating the pancreas to release insulin and increases tissue sensitivity to insulin.

II.Aim: The main of the study is to determine the sustained drug delivery system to optimize the Biopharmaceutics, Pharmacokinetic andPharmacodynamic properties of a drug in such a way that its utility is maximized through reduction of side effects and to cure the condition at shortest possible time by using smaller quantity of drug.

III. Objective: Glipizide is widely used sulphonyl urea anti diabetic agent adjunct to a set to the management of Type 2 Diabetes. Glipizide reported to have a short biological half-life (3.4 ± 0.7 hrs) requiring it to be administered in 2 to 3 doses of 2.5 mg to 10 mg per day.SR formulation that would maintain plasma levels of drug for 8 to 12 hrs might be sufficient for once-a-day dosing for glipizide SR products are need for glipizide to prolong its duration of action and to improve patient compliance.

IV. Method: The method of validation by suing the following steps
Determination of Gamma MAX of Glipizide.

- Method used for the Estimation of Glipizide in Phosphate Buffer (PH-6.8 and 0.1N.Hcl (1.2 PH).
- Preformulating studies
- API Characterization
- Organoleptic Evaluation
- Determination of Melting Point
- Solubility
- IR Spectroscopy
- Formulation of Glipizide
- Selection of Binders
- Selection of Diluents
- Selection of Polymers
- Wet Granulation Method
- Evaluation of Tablets

- By estimating Invitro drug release with EC as DCP as diluents
- By estimating Invitro drug release with combination of EC, XG as DCP as diluents
- By estimating Invitro drug release with EC, LBG as DCP as diluents
- By estimating Invitro drug release with EC as MCC as diluents
- By estimating Invitro drug release with EC & XG as MCC as diluents
- By estimating Invitro drug release with EC & LBG as MCC as diluents

V.Summary&Conclusion: The project work was entitled as "Formulation and Evaluation of SustainedRelease Matrix Tablets of Glipizide"

In this total 6 Formulations are developed using different polymers which plays a major role in sustain release.

Polymers like EC, XG& LBG are used and formulations were developed.

The formulations F6 which contains EC,LBG combination has been found to posses ideal characteristics required for Glipizide sustained release tablets than other formulations.

From this study it was concluded that F6 formulation of Glipizide sustained release matrix tablets 10 mg were developed which are suitable for once daily dosing.

The Release profiles of Glipizide sustained release matrix tablets were compared with market samples Glytop SR.

Finally, we concluded that IR studies found that there is chemical reaction takes place between the drug and Excipients.

Keywords: Anti Diabetic Drug, Formulation development of SR Drug delivery.,

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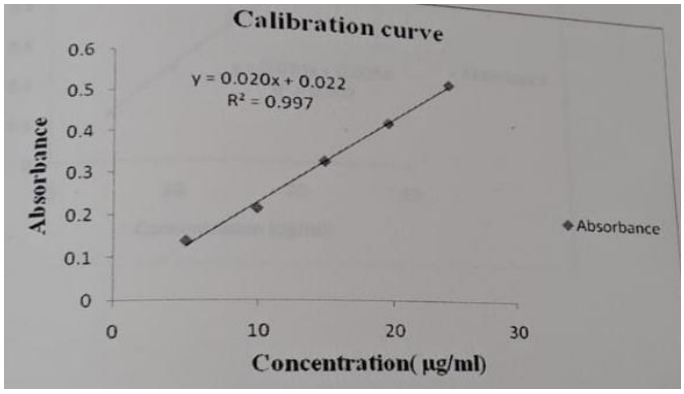
ɤ Max determination for Glipizide

Nanometers	Absorbance
210	0.551
220	0.566
230	0.533
240	0.538
250	0.208
260	0.200
270	0.253
280	0.268
290	0.142
300	0.075

Nanometers	Absorbance
271	0.265
272	0.271
273	0.275
274	0.281
275	0.287
276	0.29
277	0.287
278	0.282
279	0.276
280	0.275

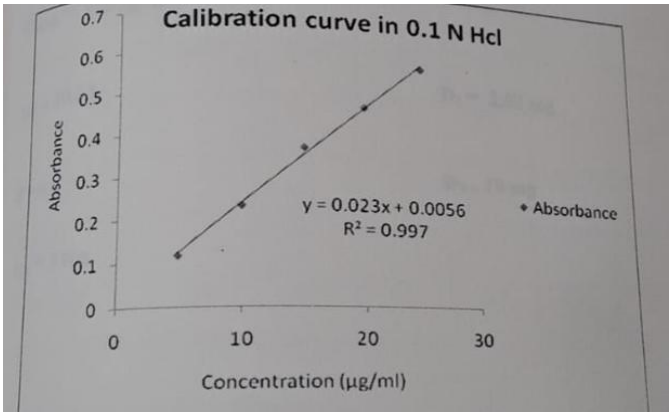
Construction of calibration curve in phosphate Buffer (Ph – 6.8)

S.no	Concentration (µg/ml)	Absorbance
1	5	0.136
2	10	0.215
3	15	0.331
4	20	0.432
5	25	0.541



Construction of calibration curve in 0.1 Hcl (Ph-1.2)

S.no	Concentration (µg/ml)	Absorbance
1	5	0.116
2	10	0.23
3	15	0.367
4	20	0.468
5	25	0.572



DOSE CALCULATION FOR 12 Hrs

D1=Cmax*Vd/F

DT=D1(1+0.693 X Time in hrs/t1/2)

Cmax = 310ng/ml
Vd=10.2L
F=0.8
T1/2 = 3 Hrs
D1=2.52 mg
DT=10 mg

Ingredients(mg)	F1	F2	F3	F4	F5	F6
Drug	10	10	10	10	10	10
Ethyl cellulose	50	25	25	50	25	25
Xanthan gum	–	25	–		25	–
LBG	–	–	25	–	–	25
PVPk30	10	10	10	10	10	10
DCP	128	128	128	–	–	–
MCC	–	–	–	128	128	128
Mg.stearate	1	1	1	1	1	1
Aerosil	1	1	1	1	1	1
Total weight	200	200	200	200	200	200

Table-16: Pre- formulation studies for lubricated granules:

EXPERIMENTAL RESULTS

Formulation code	LBD (g/cm3)	TBD (g/cm3)	Carr's index(%)	Hausner's ratio (%)	Angle of repose(o)
F1	0.59	0.64	8.37	1.08	27.2
F2	0.55	0.62	11.3	1.13	26.5
F3	0.53	0.57	7.47	1.07	27.5
F4	0.38	0.4	6.25	1.06	27.4
F5	0.3	0.36	18	1.22	25.5
F6	0.34	0.45	24.4	1.33	24.5

Table-17: Evaluation of tablet properties:

Formulation code	Diameter(mm)	Thickness(mm)	Hardness(Kg/cm2)	Tensile strength	Weight variation(mg)	Drug content (%)
F1	3.1	2.5	4.5	1.16	2.14	97.93
F2	3.1	3.2	4	0.8	3.14	96.5
F3	3.1	3.2	5	1	2.5	97.5
F4	3.1	3.15	4.5	0.92	1.02	99.38
F5	3.1	3.1	4	0.83	2.45	98.45
F6	3.1	3.1	5	1.04	2.5	95.5
M	3.1	3.2	3.5	0.7	3.45	100.9

Table-18: Comparative Dissolution Profiles for Developed Formula with DCP as Diluent:

Time in hrs	Cumulative % drug release		
	F1	F2	F3
0.5	2.44 ±0.63	0.81± 0.47	4± 0.75
1	8.56 ± 0.65	3.26± 0.23	4.7± 0.91
2	13.45 ± 0.87	4.89± 0.62	10.2± 0.92
3	17.12 ± 0.4	7.34± 0.84	6.8± 0.56
4	27.33 ± 0.57	8.97± 1.31	7.5± 1042
5	33.85 ± 0.65	11.03± 0.62	8.2± 0.84
6	34.25 ± 0.87	12.23± 1.24	12.3± 0.47
7	35.07 ± 0.38	12.64± 0.81	16.5± 0.70
8	35.89 ± 0.97	13.05± 1.22	18.5± 1.47
9	35.89 ± 0.54	17.12± 1.02	20.6± 0.81
10	36.71 ± 0.35	20.80± 1.54	24.7± 0.62
11	39.96 ± 0.40	24.47± 1.23	26.1± 1.02
12	46.90 ± 0.71	26.51± 1.02	27.2± 0.62

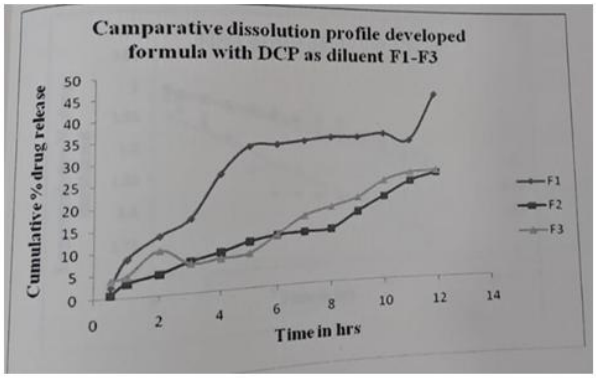


Figure-13: Comparative Zero Order Plots for F1-F3 Formulations:

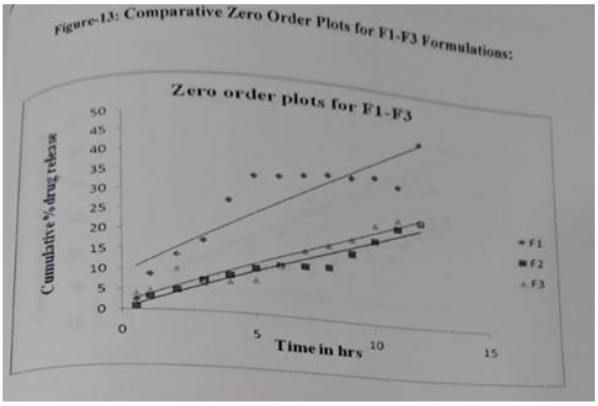


Figure-14: Comparative First Order Plots for F1-F3 Formulations:

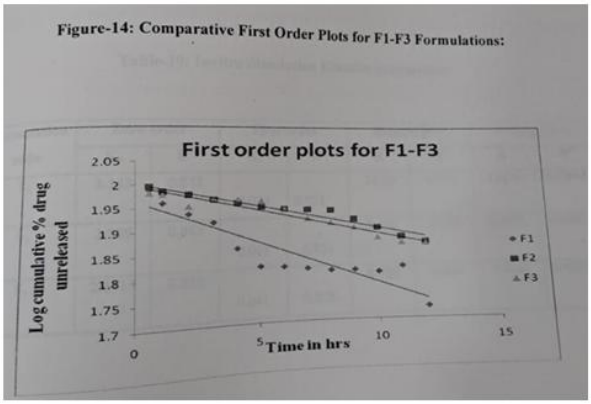


Figure-15: Comparative Higuchi Plots for F1-F3 Formulations:

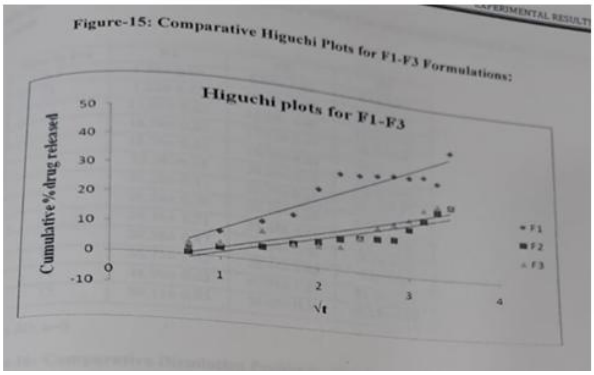
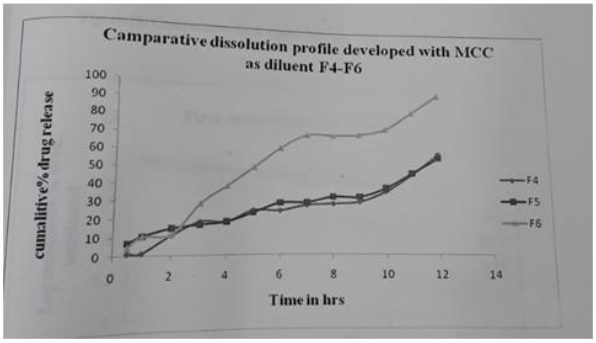


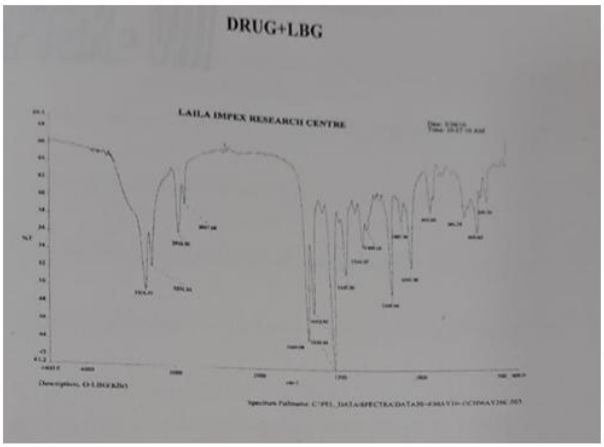
Table-19: Invitro dissolution Kinetics parameters:

Formulation code	Zero order		First order		Higuchi plot		Peppas plots	
	K_0	R^2	K_1	R^2	K	R^2	n	R^2
F_1	3.142	0.832	0.023	0.851	14.20	0.914	0.8878	0.900455
F_2	2.026	0.963	0.023	0.951	8.512	0.913	0.9570	0.960271
F_3	2.1117	0.933	0.041	0.928	8.738	0.854	1.0365	0.961791

Table-20: Comparative In vitro Dissolution Profiles For Developed Formula With MCC as Diluents

Time in hrs	F4	F5	F6
0.5	1.22± 0.94	6.93± 1.02	4.4± 0.47
1	1.22± 0.41	10.60± 0.81	10.2± 1.31
2	11.01± 0.62	15.09± 0.60	11.4± 0.62
3	18.76± 0.23	17.13± 0.47	28.9± 0.47
4	18.76± 0.81	18.76± 0.23	39.2± 1.24
5	25.28±0.23	24.06± 0.62	50.2± 0.81
6	25.28± 0.41	29.77± 0.23	61.9± 0.47
7	28.54± 0.70	30.18± 1.31	69.9± 0.81
8	29.36± 1.31	33.44± 0.47	69.9± 0.62
9	30.58± 0.47	33.44± 0.94	70.5± 0.23
10	36.71± 1.43	38.74± 0.84	74± 0.53
11	46.90± 0.62	47.71± 1.24	84.3± 0.46
12	59.13± 0.05	56.69± 0.62	95.05± 0.35





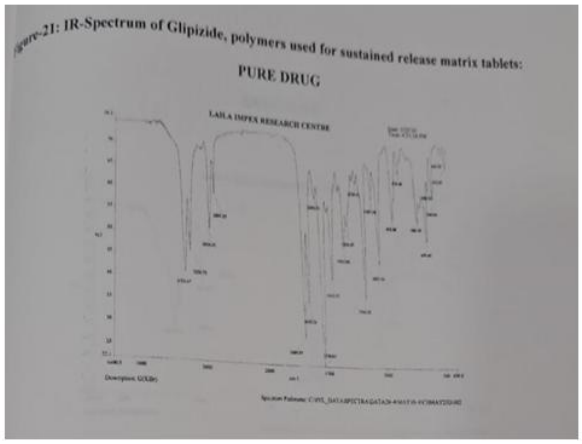
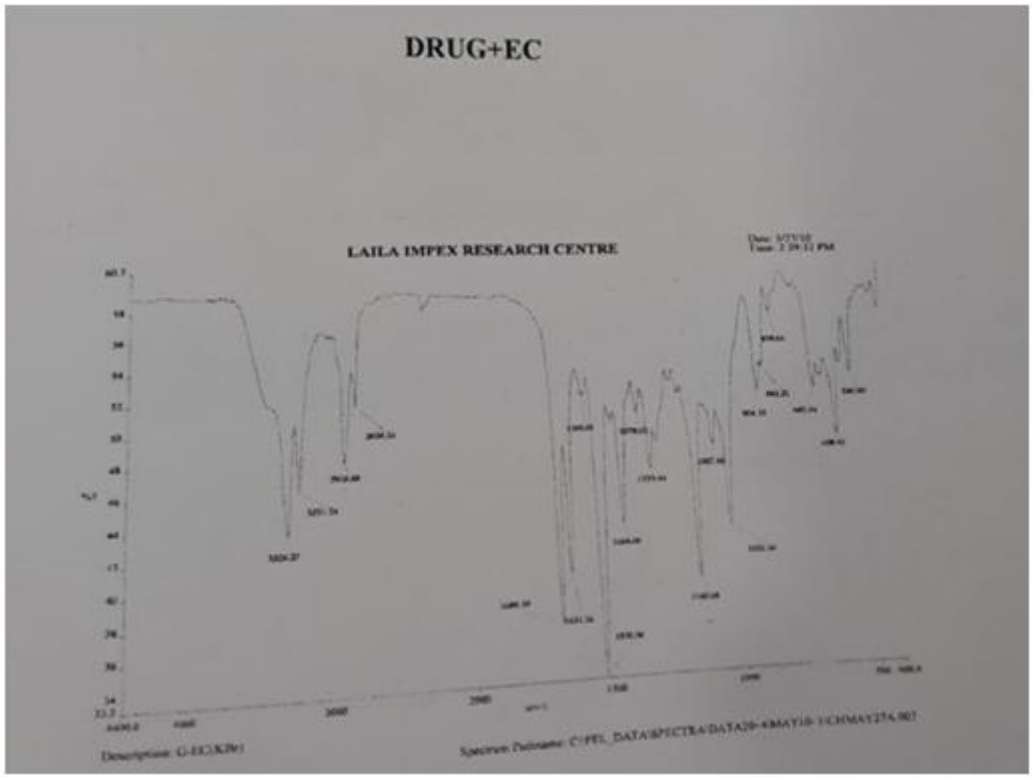


Figure-21: IR-Spectrum of Glipizide, polymers used for sustained release matrix tablets:

PURE DRUG



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